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HETA 86-350-1815 JULY 1987 BARR RUBBER CORPORATION SANDUSKY, OHIO NIOSH INVESTIGATORS: Richard L. Stephenson, I.H. Suresh Gupta, M.D., MPH Ruth Rondinelli, M.D., MPH

# I. <u>SUMMARY</u>

On May 6, 1986 the National Institute for Occupational Safety and Health (NIOSH) was requested to evaluate five workers at the Barr Rubber Corporation in Sandusky, Ohio, who had developed methemoglobinemia (in excess amounts methemoglobin reduces the available oxygen to the tissues) on April 23, 1986, while manufacturing automotive rubber bumper strips. The request was prompted by the employees' reported symptoms of yellowing of the hands, cyanosis of the lips and nailbeds, headache, dizziness, nausea, chest pain, confusion and difficulty in concentration. One of these workers reportedly passed out and suffered a seizure at the plant. Following the incident, Barr Rubber voluntarily discontinued the affected plant operations until the cause of the illnesses could be found and remedied.

On May 7-8, 1986, NIOSH investigators conducted an initial survey at the plant. The affected worker's jobs involved manually placing adhesive coated metal parts into the rubber molds without using gloves. Bulk samples of these adhesives were analyzed by NIOSH for organics. Dinitrobenzene, a chemical known to be a potent methemoglobin former and known to impart a yellowish discoloration with skin contact, was identified both qualitatively and quantitatively by two chemical analytical methods [gas chromatography and mass spectrometry (GC/MS) and infrared spectroscopy (IR)] in one bulk lot of the adhesive (Thixon 511-T) at a concentration of one percent by weight.

On May 19, 1986, the company restarted the steam press molding operations using a replacement adhesive (Thixon 521). NIOSH conducted a follow-up survey on this date to monitor the workers for signs of cyanosis (a bluish discoloration due to deficient oxygenation of the blood) or other pertinent adverse health effects and to collect pre- and post-shift venous blood samples to determine methemoglobin levels. Nine "exposed" employees and six "controls" (unexposed Barr personnel) participated in the NIOSH medical evaluation. The methemoglobin concentrations found in both the pre- and post-shift blood samples of exposed employees and controls were within normal limits (one percent or less) with a range of 0.1-1.0 percent and a mean of 0.28 percent and 0.35 percent, pre- and post-shift, respectively. None of the workers complained of any symptoms during or at the end of the work shift and physical examination revealed no signs of cyanosis.

On the basis of the data obtained during this investigation, we determined that a health hazard existed at the Barr Rubber Corporation due to dermal exposure to an adhesive (Thixon 511-T) that contained 1,4-dinitrobenzene. The affected workers' symptoms, including methemoglobinemia and cyanosis, were characteristic of exposure to dinitrobenzene, and chemical analysis of the adhesive documented its dinitrobenzene content as being one percent by weight. Subsequent laboratory analysis of the replacement adhesive has shown only trace and nondetectable quantities of dinitrobenzene and biological monitoring for methemoglobin levels in exposed workers revealed normal concentrations. Measures to prevent future incidents such as this one and to improve working conditions at Barr Rubber are recommended in Section VII of this report.

KEYWORDS: SIC 3069 (Fabricated Rubber Products), 3714 (Motor Vehicle Bumpers): adhesives, benzene derivatives, rubber workers, methemoglobin, methemoglobinemia, cyanosis, dinitrobenzene.

## II. INTRODUCTION AND BACKGROUND

On April 23, 1986, five steam press rubber molding workers of the Barr Rubber Corporation became ill while at work and were sent to the emergency room of the Firelands Community Hospital in Sandusky, Ohio. One of these workers reportedly suffered a seizure at the plant. According to the hospital records, the workers' symptoms included yellow discoloration of the palms of the hands, blue discoloration of the lips and nailbeds, headache, nausea, chest pain, dizziness, confusion, difficulty in concentration and syncope. Their blood (arterial) methemoglobin levels ranged from 3.8% to 41.2% (normal is 1% or less). Three of these five workers, who had methemoglobin levels between 25.5% and 41.2%, were treated with intravenous methylene blue and 100% oxygen. They were admitted to the hospital for observation and were discharged over the next three days. All five workers responded well to treatment, and had no complication throughout their stay in the hospital.

The affected workers used an adhesive (Thixon 511-T made by Dayton Chemicals Division, Whittaker Corporation) to bond metal studs into automotive rubber bumper strips. Without using gloves, they manually placed these adhesive coated metal studs into the rubber molds in steam powered presses prior to vulcanization. Prior to use in the steam press area, the metal parts were degreased with trichloroethylene, then spray painted with the adhesive in a paint booth and dried in an infrared oven. Although portable pedestal fans were available for use in the steam press area, none of the presses were equipped with local exhaust ventilation.

Barr Rubber had been utilizing Thixon 511-T for a number of years without problems. Prior to the incident, the last barrel (Lot # 6171) of Thixon 511-T the company had received for use in the rubber molding operation was on April 5, 1986. The company (Barr) voluntarily ceased steam press rubber molding proceses utilizing these adhesive coated studs on April 23, 1986, after the workers became ill. In an attempt to discover the cause for the workers' acute illnesses, Barr Rubber management officals requested representatives from the adhesive supplier (Dayton Chemical, Whittaker Corporation), the Occupational Health and Safety Administration (OSHA) and the Ohio Industrial Commission to conduct site visits at the plant. On April 28, 1986, one steam press, utilizing these adhesive coated studs, was operated by one plant supervisor for approximately two hours, so that an industrial hygienist with the Industrial Commission could take air samples. This supervisor then had a blood sample drawn for methemoglobin analysis. He had a reported methemoglobin level of 12.5% (normal ≤ 1%).

On May 6, 1986, NIOSH received a request from the Plant Manager of the Barr Rubber Corporation to conduct a health hazard evaluation. On May 7-8, 1986, NIOSH conducted an initial environmental/medical survey. On May 9, 1986, the NIOSH investigators made a verbal report of what they believed to be the cause of the workers' illnesses to representatives of Barr Rubber and Dayton Chemicals Division. A follow-up environmental/medical investigation was conducted on May 19, 1986, and an interim report-letter was issued on May 29, 1986, which described the findings of the bulk sample analyses and included recommendations on recall of the adhesive and advised medical evaluations for exposed workers.

## III. EVALUATION DESIGN, METHODS and RESULTS

On May 7, 1986, NIOSH investigators conducted an initial environ-mental/medical survey at the plant. Activities accomplished during the initial survey included an opening conference, a walk through of the steam press area for familiarization with job processes and materials used, and collection of pertinent Material Safety Data Sheets. In addition, photographs of the work area were taken and numerous bulk samples were collected.

## A. Environmental

Various bulk samples of the adhesives used at Barr Rubber were analyzed in early May 1986 for organics, both qualitatively and quantitatively, by gas chromatography and mass spectrometry (GC/MS) and infrared spectroscopy (IR). Since the cause of the workers' illnesses was still undetermined and the steam press molding line was not operational, a high priority and fast tumaround time was placed by NIOSH on the laboratory analytical work. Initially, the analytical work centered on two bulks; an old (lot #6171 of adhesive that was used on April 23, 1986 at the factory) and a new (a subsequent lot of adhesive) sample of Thixon 511-T.

Portions of the old bulk of 511-T were extracted with carbon disulfide (CS<sub>2</sub>) and methanol. The carbon disulfide extract was also filtered prior to analysis. All extracts were screened by a gas chromatograph equipped with a flame ionization detector (FID) using a 30 meter DB-1 fused silica capillary column (splitless mode). The CS<sub>2</sub> and methanol extracts from the old 511-T had identical chromatograms, so only the CS<sub>2</sub> extract was further analyzed by GC/MS.

Para-dinitrobenzene was identified in the old 511-T. Because the workers' symptoms appeared to be associated with exposure to this batch of Thixon 511-T, all analytical work was directed towards dinitrobenzene. Another GC equipped with a 30 meter DB-WAX column was set up to analyze for and quantitate dinitrobenzene in the old and new 511-T bulks. Two milliliter (ml) portions of old and new 511-T bulks were weighed and extracted with 5 ml of acetone. Standards of dinitrobenzene in acetone were used for comparison. Dinitrobenzene was also detected in the new (probably lot #6231) 511-T bulk adhesive. A standard of 1,4-dinitrobenzene was obtained and GC retention matched that of the samples. However, the concentration of p-dinitrobenzene in the old (diluted with toluene) bulk of 511-T was estimated to be about 30 times more than the amount of p-dinitrobenzene found in the new (undiluted) bulk of 511-T. The amount of p-dinitrobenzene was about 1% w/w in the old 511-T acetone extract but only about 0.06% w/w (0.03% if the 1:1 toluene dilution factor is figured in the results) in the new bulk of 511-T. No dinitrobenzene was detected in either the bulk toluene (used for dilution of the adhesive) or in the acetone extract of the bulk sample of Thixon 521 (probably lot #6161:the substitute bonding agent that Barr Rubber proposed to use in place of Thixon 511-T).

Upon notifying the Whittaker Corporation, Dayton Chemicals Division on May 9, 1986, of the dinitrobenzene finding, it was learned that the actual curing agent that was supposed to be in Thixon 511-T was a proprietary raw material (which Dayton purchased from the Sandoz Chemicals Corporation) rather than 1,4-dinitrobenzene. Therefore, standards of the proprietary raw material were obtained and an infrared (IR) spectroscopic analysis was performed to see if the raw material could be detected in either the old or new bulks of Thixon 511-T. A portion of both bulk adhesives (old and new Thixon 511-T) were placed on a KBr salt plate as a thin film and the solvent was allowed to evaporate. An IR spectrum was taken of each sample. Although the carbon black in the samples was highly scattering, usable spectra were obtained. The spectrum of the film of the old and new bulks of 511-T contained all the absorbance peaks of the trade secret ingredient, clearly indicating its presence in both batches. In an effort to provide some estimate of the relative quantities of the proprietary ingredient to that of 1,4-dinitrobenzene in the old bulk of Thixon 511-T, KBr pellets containing weighed portions of each compound were prepared to estimate the response of the IR absorbance peaks per mass of compound. Based on these spectra, the old bulk adhesive sample had similar amounts of both of these compounds. Subsequent IR analysis on the replacement adhesive Barr Rubber intended on using revealed much lower levels of the trade secret raw material and no detectable concentrations of 1,4-dinitrobenzene. Furthermore, chemical analyses completed on subsequent sample lots of Thixon 511-T received from Barr Rubber showed only trace and nondetectable amounts of dinitrobenzene.

## B. Medical

On the initial survey (May 7-8, 1986) a NIOSH medical officer interviewed several Barr Rubber employees including four of the five who were taken to the hospital on April 23, 1986. The fifth worker affected refused to participate in the interview process. According to the interviews, initial symptoms among Barr workers were first noted on April 18, 1986.

On May 19, 1986, the company restarted the steam press molding operations using a replacement adhesive (Thixon 521). We conducted a follow-up survey on this date to monitor the workers throughout the day for signs of cyanosis or any other pertinent adverse health effects. In addition, pre- and post-shift venous blood samples were collected to ascertain if the new adhesive increased methemoglobin levels. A total of nine exposed workers and six controls participated in the examination. Six of the exposed employees worked on the presses that deployed metal parts that had been previously spray painted with the adhesive, and the remaining three workers were those who had actually performed the spraying of the adhesive three days earlier. The controls were chosen from the office staff who had no chemical exposures. The cases and the controls were closely matched for age, sex and race.

Five cubic centimeters of venous blood were collected on May 19, 1986 in a heparinized (an anti coagulant compound) syringe from each of the 15 participants both before and after the work shift. The mouth of the needle was blocked with the help of a rubber cork so that no gases would escape. These samples were then placed on ice and transported on ice to the Cardiopulmonary Service Laboratory of the Firelands Hospital in Sandusky, Ohio and analyzed within 45 minutes of collection. The measurements for methemoglobin were done on a Co-Oximeter made by Instrumentation Laboratory in Boston, Massachusetts. This instrument provided a battery of information on each blood sample. Besides information on methemoglobin levels, we received results on hemoglobin, oxy-hemoglobin, carboxy-hemoglobin and oxygen concentration. Laboratory normals were: 14-18 grams of hemoglobin per 100 ml of blood for men, and 12-16 grams of hemoglobin per 100 ml of blood for women; the oxy-hemoglobin concentration of 85-98 percent for arterial blood, and 65-85 percent for venous blood; carboxy-hemoglobin concentration of 0-3 percent under normal breathing conditions.

The methemoglobin concentrations measured on May 19, 1986 in both the pre- and post-shift blood samples were within normal limits with a range of 0.1-1.0 percent and a mean of 0.28 percent and 0.35 percent, pre- and post-shift, respectively. Hemoglobin and carboxy-hemoglobin values were within the normal range also. The mean hemoglobin concentration was 17.2 gram percent (range 12.5-20.2) and 16.4 gram percent (range 13.6-19.5), pre- and post-shift respectively. The mean carboxy-hemoglobin concentration was 2.9 percent (range 0.4-8.2) and 3.3 percent (range 0.7-9.0), for pre- and post-shift respectively. None of the workers complained of any symptoms during or at the end of the work shift, and no cyanosis was noted upon physical examination.

# IV. EVALUATION CRITERIA

## A. Environmental Criteria

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or a hypersensitivity (allergy).

In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the evaluation criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, and thus potentially increase the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent become available.

The primary sources of environmental evaluation criteria for the workplace are: 1) NIOSH Criteria Documents and Recommended Exposure Levels (RELs), 2) the American Conference of Governmental Industrial Hygienists' (ACGIH) Threshold Limit Values (TLVs), and 3) the U.S. Department of Labor (OSHA) occupational health standards. Often, the NIOSH RELs and ACGIH TLVs are lower than the corresponding OSHA standards. Both NIOSH RELs and ACGIH TLVs usually are based on more recent information than are the OSHA standards. The OSHA standards also may be required to take into account the feasibility of controlling exposures in various industries where the agents are used; the NIOSH RELs, by contrast, are based primarily on concerns relating to the prevention of occupational disease. In evaluating the exposure levels and the recommendations for reducing these levels found in this report, it should be noted that industry is legally required to meet those levels specified by an OSHA standard.

A time-weighted average (TWA) exposure refers to the average airborne concentration of a substance during a normal 8- to 10-hour workday. Some substances have recommended short-term exposure limits or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from high, short-term exposures.

# A. Respiration, Hemoglobin & Methemoglobin

The basic activity of the respiratory system is to supply oxygen and exhaust carbon dioxide. The blood via erythrocytes (red blood cells) transports the oxygen from the alveoli of the lungs to peripheral tissue where it is used to support aerobic metabolism. Thirty percent of the weight of red blood cells consists of hemoglobin (Hb). Hemoglobin, the red pigment in erythrocytes, contains 34% iron and is metabolized from three major components: a porphyrin, an oligomeric protein (globulin), and an atom of iron in the ferrous state. Hemoglobin combines with four molecules of oxygen to produce a loose complex (oxygen-carrying hemoglobin or oxy-hemoglobin-HbO<sub>2</sub>) which easily dissociates on delivery to the vicinity of oxygen demand.(1,2,3) In oxygenated blood there is a continuous tendency for the ferrous iron in the hemoglobin molecule to be oxidized to the ferric state (HbFe+++) producing methemoglobin (MHb), a chocolate brownish colored compound which darkens the blood. The ferric ion cannot accept oxygen because the iron is bound tightly to a hydroxyl group or to some other anion. Fortunately in most people an enzyme system exists that reduces MHb as rapidly as it is formed back to normal Hb.(2,4,5) Normally the methemoglobin is

continuously reduced by the enzyme NADH diaphorase (methemoglobin reductase) and cytochrome. However, either a marked reduction of the NADH diaphorase or an increase in the oxidation of hemoglobin will result in the accumulation of MHb and a condition known as methemoglobinemia.(6) Exactly how methemoglobin is formed is not yet clearly understood. Many researchers have studied the mechanism, but no one has offered a universally accepted hypothesis because the findings of the in vivo studies have not always agreed with the results of the in vitro evaluations.(7,8)

The concentration of MHb usually found in the body (erythrocytes) is 1% or less.(3,6,9) The presence of MHb has two potentially adverse effects, the severity of which is commensurate with its concentration:

- 1) the hemoglobin that has been oxidized to MHb is no longer able to transport oxygen to help meet the body's needs, thus a situation similar to that of anemia results and;
- 2) the remaining HbO2 (or ferrous ions) have a greater affinity for oxygen since the presence of MHb in the blood incapacitates the hemoglobin's normal functions; oxygen is unloaded less readily in the tissues. (10,11)

# B. <u>Cyanosis & Aromatic Nitro Compounds</u>

When the oxygen supply is unable to meet tissue demand or when the cells are unable to utilize the available oxygen, a state of hypoxia will develop and a bluish-grey discoloration or cyanosis of the skin, fingernail beds, ear lobes, nose, lips and mucous membranes of the body occurs.(2,5,12,13) However, the absence of cyanosis symptomatology may be deceiving. Usually, evidence of blue lips and fingernail bases is considered a foundation for diagnosis, but several cases have been found which gave no prior visible evidence.(1)

Cyanosis is a sign of tissue oxygen deficiency and occurs when the  $HbO_2$  level falls below the critical oxygen demand level. A deficiency of oxygen in the blood stream can be produced by several conditions.

- 1) Insufficient respiratory oxygen pressure (concentration), for example, anoxia experienced by workers in poorly ventilated environments where oxygen has been displaced by inert gas or consumed by combustion. In addition, an obstructive breathing problem (e.g.asthma) or a mechanical interference (e.g.choking or strangulation) will deprive the blood of oxygen.
- 2) Impaired blood circulation (e.g. conditions which prevent free circulation of the blood through the lungs, or permit circulation to bypass the heart such as a pulmonary embolism or a septal defect in the heart) and,
- 3) Invasion of the blood stream by chemicals that displace oxygen or block the reaction between hemoglobin and oxygen. These materials can be divided into three general categories: a) the reactive gases and vapors that are inhaled such as CO, H<sub>2</sub>S, N<sub>2</sub>O<sub>3</sub>, HCN, nitrobenzene, aniline, etc., and b) ingestion of compounds such as nitrates, nitrites, sulfides, and some medicinals such as sulfanilamide, acetanilide, etc., and c) absorption of the fat-soluble liquids and solids such as the aromatic nitro or amino compounds many of which can easily penetrate through the skin.(2,14) An additional list of some of the chemicals and drugs that are associated with methemoglobin production has been included as Appendix I.

Associated symptoms of chemically-induced cyanosis may include nausea, dyspnea, headache, dizziness, listlessness, sudden blackouts, unconsciousness, coma, and possibly even death from severe exposure to the materials listed in #3 above.(1,10)

Temperature has a rather clear-cut effect on the incidence of industrial chemical cyanosis and methemoglobinemia: i.e., the frequency increases as a linear function of ambient temperature. Therefore, the frequency rate usually reaches a peak during the summer and then falls off during the winter.(1,2,11,14,15). Some of the factors leading to increased skin absorption of the aromatic nitro compounds, for example, increased peripheral vasodilation and perspiration, and not wearing protective gloves, may be somewhat seasonally related. Exceptions to this seasonal variation rule are not uncommon. Cyanosis from lesser exposures often develops rapidly under conditions of elevated ambient temperature, in drier rooms, near steam sills, etc., or when not wearing protective gloves.(1,2,16)

The aromatic nitro compounds are headed by nitrobenzene ( $C_6H_5NO_2$ ) and are derived from benzene and its homologues (toluene and xylene), or naphthalene and anthracene by substituting a nitro group ( $NO_2$ ) for one or more hydrogen atoms directly on the benzene ring. The nitro group is generally introduced into the benzene ring by direct nitration in a mixture of sulfuric and nitric acids in proportions suited to the reactivity of the system.(11) Aromatic nitro compounds like para-dinitrobenzene (p-DNB) are used in the manufacture of dyes, explosives, pigments, insecticides, textiles, plastics, resins, elastomers, photographic developers, pharmaceuticals, plant-growth regulators, fuel additives, rubber accelerators and antioxidants.(13,11)

It is a well documented occupational hazard that exposure to any of several aromatic nitro compounds can result in systemic poisoning. Specific characteristics of these compounds are that most are very readily absorbed through the skin, have as an acute potential health hazard cyanosis and methemoglobinemia, and as a chronic hazard, anemia.(1,2,6,9,11,17) Linch (2,14) refers to the overall effect as the "cyanosis-anemia syndrome" and has ranked 13 potent industrial chemical cyanosis/anemia producers according to their biochemical potentials as shown in Table #I below:

# Table #I RELATIONSHIP BETWEEN CAUSATIVE AGENT AND BIOCHEMICAL POTENTIAL

(Ranked in descending order of relative toxicity: #1 most, #13 least potent)

| <u>CHEMICAL</u>          | CYANOTIC RANK | ANEMIC RANK | <u>OVERALL RANK</u> |
|--------------------------|---------------|-------------|---------------------|
|                          |               |             |                     |
| ortho-chloroaniline      | 1             | -           | -                   |
| <u>dinitrobenzene</u>    | 2             | <u>5</u>    | 1                   |
| meta-nitroaniline        | 3             | -           | -                   |
| para-toluidine           | 4             | 4           | 4                   |
| nitrobenzene             | 5             | 1           | 2                   |
| meta-toluidine           | 6             | 12          | 8                   |
| ortho-nitrochlorobenzene | 7             | -           | -                   |
| aniline                  | 8             | 10          | 10                  |
| para-dinitrosobenzene    | 9             | 11          | 11                  |
| ortho-toluidine          | 10            | 8           | 9                   |
| ortho-nitrotoluene       | 11            | -           | -                   |
| nitronaphthalene         | 12            | 13          | 13                  |
| dichloroaniline          | 13            | 6           | 12                  |

Cyanogenic potential is profoundly altered by both the nature and position of substituent groups in the benzene ring (e.g.para-toluidine vs ortho-toluidine or meta-toluidine: see Table #I above).(11) Evans (18), Linch (2,14) and others (7) believe that most of the aromatic nitro and amino compounds probably are not cyanosis producers themselves but are converted (via biochemical oxidation-reduction enzyme systems) into some active cyanogenic metabolites that cause complete oxidation of hemoglobin (ferrous to ferric) and hinder oxygen transport to the tissues. As discussed earlier in this report, under normal circumstances hemoglobin is very loosely connected to oxygen without causing true oxidation.(7)

# C. 1,4-Dinitrobenzene

# 1) <u>Chemical and Physical Properties</u>

1,4-Dinitrobenzene, also known as para-dinitrobenzene (p-DNB),  $C_6H_4N_2O_4$ , chemical abstract service registry number (CAS) 100-25-4, is a pale yellow solid (crystal) that is soluble in acetone, acetic acid and toluene.(6,13,19) The vapor pressure of all three DNB isomers is low (less than 1 mm Hg at  $20^{\circ}\text{C}(68^{\circ}\text{F})$ .(13)

# 2) <u>Toxicological Effects</u>

Dinitrobenzene is readily absorbed through the skin either as a solid, liquid, or vapor and may cause a yellowish discoloration to the eyes, hair, and skin.(13,20,21) Even a small amount absorbed from contaminated clothes or shoes may cause toxic symptoms.(13) As shown in Table #I, dinitrobenzene is ranked #1 overall in the cyanosis-anemia classification and #2 among the cyanosis producing chemicals. P-DNB is an outstanding methemoglobin former which appears to be its primary effect when it is absorbed.(5,6,7,8,10,14) Some of the potential health effects of exposure to dinitrobenzene include: cyanosis and headache (greater than 15% MtHB), dizziness and fatigue (greater than 40%), ataxia, shortness of breath upon mild exertion, tachycardia, nausea, vomiting and drowsiness (up to 70%), and stupor, coma, and possibly death (greater than 70%).(13,22) Chronic exposure to dinitrobenzene has been reported to cause respiratory initation, liver damage, visual impairment (reduced visual acuity and central scotomas, particularly for red and green colors), and hearing loss.(6,13,23) The consumption of alcohol has been reported to aggravate the toxic effects of dinitrobenzene.(13)

# 3) Dinitrobenzene Exposure Criteria

The current federal OSHA PEL (24) and ACGIH TLV (25) for dinitrobenzene (all isomers) is one milligram per cubic meter of air (mg/m³) or 0.15 parts per million (ppm) based on an eight-hour TWA which includes a skin notation (substances which can be absorbed cutaneously and thus contribute to the overall exposure). Sweden, East and West Germany, Czechoslovakia and the USSR have all adopted this value. The basis for setting the limit for dinitrobenzene was, moreover, an estimate of the relative toxicities of the polynitro aromatic compounds compared to those of the mononitro derivatives.(25) Unfortunately, there are few if any published reports in the occupational literature concerning measured levels of exposure to dinitrobenzene and health effects which are experienced at these levels.

## V. DISCUSSION and CONCLUSIONS

Although no direct measurement of worker's exposures to p-dinitrobenzene at Barr Rubber was documented, the collected data strongly implicates dinitrobenzene as the primary causative agent for the illnesses because 1) there were no readily apparent changes in work processes or materials used at the plant prior to the incident, 2) other workers with similar jobs in adjacent areas to the steam press molding operations in the plant, using several like materials except for the adhesive, did not experience ill health effects, and 3) all the symptomatic employees exhibited characteristic signs of dinitrobenzene poisoning. As explained earlier in this report, if during the manufacture of the trade secret raw material, proper quality control procedures are not followed, it is quite possible to have 1,4-dinitrobenzene as a by-product and two analytical laboratories (NIOSH and Sandoz), found dinitrobenzene in the bulk adhesive. Following replacement of the dinitrobenzene-containing adhesive, there was no recurrence of methemoglobinemia in any of the production workers. What contribution the proprietary raw material had in causing the symptoms could not be determined.

The absence of any significant airborne contaminants during the exposure simulation study conducted on April 28, 1986, was not surprising, since many of the nitrobenzene derivatives have low vapor pressures and do not contribute an airborne hazard under normal ambient temperatures.(11,14) The main route of entry into the body for several of these fat-soluble cyanogenic aromatic nitro compounds, including dinitrobenzene, is by skin absorption.(2,26)

Following the incident at Barr Rubber both Dayton Chemicals and the Sandoz Corporation revised their Material Safety Data Sheets for Thixon 511-T and the trade secret raw material. Dayton Chemical now lists that "trace amounts of dinitrobenzene which can cause cyanosis may be present" and Sandoz states that the proprietary ingredient ...,"has been known to cause an increase in methemoglobin." Prior to the printing of this report the Sandoz Chemicals Corporation decided to discontinue the manufacture of the raw material, and Barr Rubber moved their operations from Sandusky, Ohio to Coshocton, Ohio. As a note of interest, we contacted Dayton Chemicals Division on May 9, 1986 to inform them that dinitrobenzene had been detected in the Thixon 511-T lot used on April 23, 1986, at Barr Rubber Corporation and of the potential lethal impact this situation posed. At that time, we requested the identity of all customers that may have received this same lot so that a warning could be issued. Although we were denied this information, on May 23, 1986, two weeks after the NIOSH notification, Dayton Chemicals Division did issue a written recall notice to their Thixon 511-T customers for two lots of Thixon 511-T (lots #6171 and #6231). The general text of the recall notice/letter is included in this report as Appendix II.

On May 20, 1986, Dayton's supplier of the curative system (which contains the trade secret raw material from Sandoz Corporation) used in Thixon 511-T verbally acknowledged to NIOSH of finding dinitrobenzene (via their laboratory analysis) in lot #8001 (Dayton's lot #6171) which was used to make Thixon 511-T and revealed finding dinitrobenzene in other lots (besides #8001) of their curing agents. Since Sandoz, up to the time of the incident at Barr Rubber, reportedly did not routinely retain representative raw material lot samples for future chemical analysis, nor did they routinely analyze their proprietary curing agents or raw materials for dinitrobenzene content, (nor did Dayton Chemical), the potential for dinitrobenzene to be found in significant quantities in other lots of the curing agents supplied to Dayton Chemical for use in making adhesives, apparently did exist. Therefore, in the interim report-letter issued to Dayton Chemical in May 1986, (attached as Appendix III) we strongly encouraged them to track other lots of bonding materials supplied to their customers to ensure that additional workers were not exposed to this potentially lethal agent. We believed that the occupational health considerations dictated the following immediate actions:

- Dayton Chemicals should promptly advise their customers to stop usage of Thixon 511-T (lot 6171) and recall this material.
- 2) Dayton Chemicals should advise their customers who purchased Thixon 511-T (lot 6171) to provide medical evaluations for presently exposed workers who may have utilized this material. These evaluations should include:
  - a) Personal medical interviews designed to solicit histories of symptoms compatible with methemoglobinemia,
  - b) Physical examinations with special attention to dermal (yellowish) discoloration and blue coloration of the lips, tongue and fingernails, and

c) Collection of post-shift venous blood samples to determine methemoglobin levels and liver function enzymes. It should be kept in mind that signs and symptoms of methemoglobinemia may not appear until 15 percent or more of hemoglobin has been converted to methemoglobin. Therefore, blood samples for methemoglobin analysis are necessary to rule-out low grade exposures. d)Prudence would dictate that all purchasers of the adhesive be notified of the dinitrobenzene problem and that the same medical evaluations outlined above be conducted by each purchaser of the adhesives in question (unless proven otherwise by chemical analysis), and not only purchasers of Thixon 511-T Lot #6171.

We did not find any reference in the occupational health literature of any long-term health effects from acute exposure to dinitrobenzene. Industrial related illnesses such as those experienced at Barr Rubber, can be prevented and the severity of reactions can be reduced in the future by making employers and employees aware of the chemical and physical properties (including possible end-products and by-products (actual and potential) from chemical reactions that could occur) and the potential health effects of the materials they work with, and by making sure they understand the need for appropriate protective equipment (e.g.gloves) when necessary.

# VII. <u>RECOMMENDATIONS</u>

In view of the findings of this investigation, the following recommendations are made to ameliorate existing or potential hazards and to provide a better work environment for the employees covered by this determination.

- 1. A continuing education program conducted by a person or persons qualified by experience or special training should be instituted and offered on a regular basis to ensure that all employees have current knowledge and understanding of the job safety and health hazards, including the potential health problems associated with exposure to the materials used at the plant, the methods of protection utilized and proper work practices. Supervisors and their employees should familiarize themselves with product manufacturers' recommendations regarding precautionary measures and specific directions before attempting to use any materials in the conduct of their work.
- 2. Current Material Safety Data Sheets (MSDS) and all available information concerning products used should be obtained and made available to all potentially exposed personnel.
- 3. If the raw material continues to be used as an ingredient in the adhesive manufacturing process, the following recommendations should be adhered to. Also, should any other potential methemoglobin-producing chemical be used as a curing agent in the adhesive (see Appendix I), similiar concepts as presented below for dinitrobenzene and other chemicals should be followed:
  - a. The raw material supplier and the adhesive manufacturer should incorporate and follow sufficient quality control procedures in their chemical manufacturing processes that would closely monitor the oxidation processes and include analytical testing (for every batch of curing agent and adhesive made) for dinitrobenzene (e.g.GC/MS bulk analyses) and proprietary raw material (IR bulk analyses) content so as to ensure that excessive quantities of dinitrobenzene and other methemoglobin-producing compounds are not present.

- b. Use of <u>butyl rubber</u> protective clothing (gloves, overshoes, forearm sleeves and aprons) can help reduce exposures when handling dry coated parts. No other fabricated commercially available elastomer approaches butyl rubber in resistance to penetration by aromatic nitro compounds. <u>Note</u>: Sandoz lists neoprene or PVC-type protective gloves on their latest raw material MSDS and Dayton Chemicals lists rubber gloves on their Thixon 511-T MSDS. Ordinary rubber fails to give complete protection against the aromatic nitro compounds and latex gloves have been shown to be permeable to dinitrobenzene.(2,6,7,27) Gloves should be of sufficient length and should be flexible enough to be used for the task to be performed.
- c. Skin contact with the adhesive should be avoided. If skin contact with the adhesive does occur, any contaminated clothing should be promptly removed and the affected area should be immediately washed with soap and warm water (shower if necessary).
- d. Periodic medical monitoring of those workers exposed to the adhesive should include as a minimum, the items listed under 2a and 2b in the Discussion and Conclusions Section V of this report (medical interviews and physical exams).
- e. Persons with pre-existing conditions of chronic anemia and/or known hemoglobinopatheis (e.g.sickle cell trait) should not be assigned work in areas where the adhesive is used.
- f. No foods, chewing gum or tobacco products should be permitted in areas where the adhesive is used.

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# X. <u>DISTRIBUTION AND AVAILABILITY OF REPORT</u>

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, Publications Dissemination Section, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days, the report will be available through the National Technical Information Service (NTIS), 5285 Port Royal, Springfield, Virginia 22161. Information regarding its availability through NTIS can be obtained from NIOSH Publications Office at the Cincinnati address. Copies of this report have been sent to:

- 1. Pretty Products Corp., Coshocton, Ohio (formerly Barr Rubber, Sandusky, Oh.)
- 2. Dayton Chemicals Division, Whittaker Corporation, Dayton, Ohio
- 3. Sandoz Chemicals Corporation, Charlotte, North Carolina
- 4. United Rubber Workers International Union
- 5. OSHA, Region V

For the purpose of informing affected employees, copies of this report shall be posted by the employer in a prominent place accessible to the employees for a period of 30 calendar days.

## APPENDIX I

# Chemicals And Drugs Associated with Methemoglobin Production

Acetanilide Nitrobenzene

Acetophenetidin (phenacetin) Nitroglycerin

o-Naphthylamine Nitrophenol

Aminophenol Witrosobenzene

Ammonium nitrate p-Aminophenol

Amyl nitrate p-Aminopropiophenone

Aniline p-Bromoaniline

Anilinethanol p-Witroaniline

Antipyrine Phenylenediamine

Arsine Phenylhydrazine

Benzocaine Phenylhydroxylamine

Bixmuth submitrate Plasmoquin

Bronates Potassium chlorate

Chloronitrobenzene Propitocaine

Dimethylamine Pyridium

Dinitrophenol Pyrogallol

Dinitrotoluene Resorcinol

Hydroquinone Sulfonal

Hydorxylacetanilide Sulfonamides

Hyroxylamine Toluenediamine

Lidocaine Toluidine

Methylacetanilide Toluylhdroxylamine

Methylene blue Trinitrotoluene

Monochloroaniline Trional



May 23, 1986

**Dayton Chemicals Division** 

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#### Dear Customer:

Your immediate attention to the following announcement is requested.

A supplier of one of the materials used to produce THIXON® 511-T notified us on May 19, 1986 that some of its material had been found to contain dinitrobenzene. Our records show that some of that supplier's material was used in lots 6171 and 6231 of 511-T.

So long as the containers from lots 6171 and 6231 remain factory sealed, there is no danger to person or property. These containers must not, however, be opened since exposure to high levels of dinitrobenzene can be harmful or fatal under certain circumstances.

Please check all inventory and place all containers of 511-T from lots 6171 and 6231 in an area where they will not be subject to use. If you will contact your local THIXON® representative, he will make all arrangements, at no cost to you, to remove those containers and deliver new material or credit your account. Should you encounter any difficulty whatsoever, you may contact me at the following telephone number: (513) 839-4612.

We very much regret having to issue this recall notice. We are doing so because we are responsible suppliers of a quality product, and your safety and confidence in our product is our greatest concern. Please he assured that only the above mentioned lots pose any similar health hazard. No other lots of 511-T contain dinitrobenzene. We have confirmed with our material supplier that the presence of dinitrobenzene was an isolated occurrence which can and will be prevented in the future.

We appreciate your confidence in our product. We pledge to you that we will continue to supply you with a quality product at a fair price.

Sincerely,

Bernard P. Speriman

President

Dayton Chemicals Division

kw

cc: Don Branek, Technical Sales impresentative

May 29, 1986 HETA 86-350

Whittaker Corporation
Dayton Chemicals Division
10 Electric Street
West Alexandria. Ohio 45381

Dear :

This letter is in reference to our conversation on May 20, 1986, and the ongoing health hazard evaluation that we are conducting at Barr Rubber Corporation in Sandusky, Ohio.

Un May 6, 1986, NIOSH received a request from to investigate an outbreak of methemoglobinemia among five of their rubber molding workers. On April 23, 1986, the hospital records of these five employees indicated that each had varying degrees of yellow discoloration of the palms of the hands, varying degrees of cyanotic (blue) discoloration of the lips, as well as methemoglobin levels ranging from 3.8% to 41.6% (normal is less than 1%) in arterial blood. One of these workers was reported to have suffered a seizure at the plant.

Methemoglobin prevents oxygen uptake by hemoglobin which then results in inadequate oxidation of body tissues. Symptoms of elevated methemoglobin levels include: cyanosis and headache (greater than 15% methemoglobin), dizziness and fatigue (greater than 40%), ataxia, shortness of breath upon mild exertion, tachycardia, nausea, vomiting and drowsiness (up to 70%) and stupor, coma and possibly death (>70%).

Dinitrobenzene, a chemical known to be a potent methemoglobin former and known to impart a yellowish discoloration with skin contact, was identified both qualitatively and quantitatively by two chemical analytical methods [gas chromatography and mass spectrometry (GS/MS) and infrared spectroscopy (IR)] in Thixon 511-T at a concentration of one percent by weight. This adhesive was being used by Barr Rubber to bond metal studs into automotive rubber bumper strips. Workers manually placed these treated metal studs, without gloves, into the rubber molds. The company had been utilizing Thixon 511-T for a number of years without incident. Barr received the dinitrobenzene containing barrel of Thixon 511-T on April 5, 1986 (Lot # 6171 from Dayton Chemicals Division, Whittaker Corporation). According to the NIOSH medical

## APPENDIX III (cont)

officer interviews, initial symptoms among Barr Rubber workers were first noted on April 18, 1986. The company voluntarily ceased rubber molding processes utilizing these adhesive coated studs on April 23, 1986, after the workers became ill. On April 28, 1986, one steam press, utilizing these adhesive coated studs, was operated by one plant supervisor for approximately two hours, so that the Ohio Industrial Commission representative could take air samples. This supervisor then had a blood sample drawn and had a reported methemoglobin level of 12.5%.

We first contacted James D. Bonfiglio, Products Manager, at Dayton Chemical Division on May 9, 1986, to inform him that we had detected dinitrobenzene in the Thixon 511-T lot used on April 23, 1986, at Barr Rubber Corporation. We informed Mr. Bonfiglio of the potential grave occupational health impact this situation posed, and therefore asked that he identify all customers that may have received other barrels from this same lot, as well as the supplier of the curing agent used in their adhesive.

On May 13, 1986, we again contacted Mr. Bonfiglio, and were given the name of the supplier of the curing agent. However, he did not give us a list of companies that purchased adhesive from lot 6171. Following this conversation, the supplier of the curing agent to Dayton Chemical was contacted. The raw mateerial supplier stated that the Dayton Chemical Lot 6171 contained curing agent from their Lot 8001. We requested that a reagent grade standard of the actual curing agent be sent to us for our analytical testing. We received this material on May 22, 1986.

On May 14, 1986, we contacted Peter Jazenski, Development Manager, Dayton Chemical Corporation and asked him to provide a reference standard of the bonding agent, which we received that same day. Mr. Jazenski also identified, at our request, component information of Thixon 521 (the substitute bonding agent that Barr Rubber proposed to use in place of Thixon 511-T).

On May 15, 1986, we again requested the names of companies which had purchased adhesive from lot 6171 from Peter Jazenski. On May 13, 1986, Denny Stout sent us a bulk sample of Thixon 521 for quantitative and qualitative dinitrobenzene analysis. These chemical analyses were completed on May 15, 1986, and they revealed no detectable quantities of dinitrobenzene in one lot of (probably #6161) Thixon 521. Chemical analyses were also completed on May 15, 1986, on subsequent sample lots of Thixon 511-T received from Barr Rubber which have shown only trace and nondetectable concentrations of dinitrobenzene.

As you recall during our conversation with you on May 20, 1986, you verbally denied our request for you to identify the names and locations of all Dayton Chemical Corporations customers who may have received any Thixon 511-T (Lot #6171). We would like to reiterate that we believe it is imperative that these customers be informed of the potential occupational health hazards which may result from its use. To allow your customers to use this material without any warning could result in unsuspecting workers suffering from potentially severe health consequences.

## APPENDIX III (cont)

There is no doubt that the 511-T bonding agent, in at least one lot (#6171) that you market, contains dinitrobenzene. On May 20, 1986, following our phone conversation your supplier of the curative system used in Thixon 511-T verbally acknowledged finding dinitrobenzene via their laboratory analysis of lot #8001 (Dayton's Lot 6171) used to make Thixon 511-T, as well as finding dinitrobenzene in other lots of their curing agents. The potential for dinitrobenzene to be found in significant quantities in other lots of the curing agents supplied to Dayton Chemical for use in making adhesives therefore apparently does exist.

Thus we believe it is essential for Dayton Chemical to track other lots of bonding materials supplied to their customers to ensure that additional workers are not exposed to this potentially lethal agent. Although there may have been chemical exposures in addition to dinitrobenzene which may have contributed to causing the symptoms to be experienced by the Barr Rubber workers, the data we have collected to date strongly implicates dinitrobenzene as the major causative agent for the illness.

In our opinion, the occupational health considerations dictate the following immediate actions:

- 1) You should promptly advise your customers to stop usage of Thixon 511T (Lot 6171) and recall this material.
- 2) You should advise your customers who purchased Thixon 511T (Lot 6171) to provide medical evaluations for presently exposed workers who may have utilized this material. These evaluations should include:
  - a) personal medical interviews designed to elicit histories of symptoms compatible with methemoglobinemia,
  - b) physical examinations with special attention to dermal (yellowish) discoloration and blue coloration of the lips, tongue and fingernails, and
  - c) collection of post-shift venous blood samples to determine methemoglobin levels and liver function enzymes. It should be kept in mind that signs and symptoms of methemoglobinemia may not appear until 15% or more of hemoglobin has been converted to methemoglobin. Therefore, blood samples for methemoglobin analysis are necessary to rule-out low grade exposures.
- Since your raw material supplier has found dinitrobenzene in other raw material lots, and has stated that they do not routinely retain representative raw material lot samples for future chemical analysis, all lots must be presumed to be contaminated by dinitrobenzene, unless proven otherwise by chemical analysis. Therefore, prudence would dictate that all purchasers of the adhesive be notified of this possibility and that the same medical evaluations outlined above be conducted by each purchaser of the adhesives in question, and not only purchasers of Thixon 511T (Lot 6171).

# APPENDIX III (cont)

We are willing to lend our industrial hygiene (including chemical analytical services) and occupational medical expertise in this situation. Should you have any questions concerning this letter you may contact us at (513) 841-4374 for R. Stephenson and (513) 841-4386 for R. Rondinelli. We would appreciate hearing of your intentions by June 3, 1986.

Sincerely yours,

Richard L. Stephenson
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